

10-15-2013

Open Door to Pharmaceutical Shortcuts: How the FDA can Regulate Race-Based Personalized Medicine

Roxanne Melvin

American University Washington College of Law

Follow this and additional works at: <http://digitalcommons.wcl.american.edu/hlp>

 Part of the [Health Law Commons](#)

Recommended Citation

Melvin, Roxanne. "Open Door to Pharmaceutical Shortcuts: How the FDA can Regulate Race-Based Personalized Medicine." *Health Law & Policy Brief* 6, no. 1 (2012): 25-33.

This Article is brought to you for free and open access by Digital Commons @ American University Washington College of Law. It has been accepted for inclusion in *Health Law and Policy Brief* by an authorized administrator of Digital Commons @ American University Washington College of Law. For more information, please contact fbrown@wcl.american.edu.

COMMENT:

OPEN DOOR TO PHARMACEUTICAL SHORTCUTS: HOW THE FDA CAN REGULATE RACE-BASED PERSONALIZED MEDICINE

Roxanne Melvin*

INTRODUCTION

On September 27, 2011 the UC Berkeley College Republicans hosted a bake sale that was splashed across headlines.¹ This sensational bake sale had a slightly different pricing scheme from the average bake sale: prices ranged from two dollars for white men to twenty-five cents for Native Americans.² If you were not in attendance for the uproar leading up to the day of Berkeley's "pay-by-race" bake sale,³ the pricing scheme may not elicit too much emotion; however, what if that were the case when you went to the pharmacy?⁴ Imagine hearing about a medication for a disease you have. You go to your physician to see if this may be a glimmer of hope for your ailment, only to feel offended. Upset and outraged, you want an explanation as you learn your physician can prescribe the drug, but since you are not black, you may have to pay more.⁵ Further inquiry reveals black patients may pay less because the drug was approved for use in black patients with heart failure.⁶

As unsettling as it may sound, that is the case if you are Caucasian, Asian, Pacific Islander, or any other race besides black, and would like to try BiDil.⁷ Naturally, the situation demands explanation when the Food and Drug Administration (FDA) approves a drug for use in a particular racial group. In light of advances in genetic science, should a company have to provide evidence as to why it thinks it is appropriate to make a drug race specific? What

are the constitutional implications for drugs approved for specific racial groups?⁸ Science is quickly advancing in the field of genetics and it is being used to diagnose and treat illnesses; what should a company be required to do to prove its actions pass constitutional muster if it wishes to use race to target recipients of its drugs instead of genetics?⁹ Finally, does the FDA have power to regulate in a way that encourages companies to expand on new scientific discoveries while not depriving certain patients of life-saving treatment when the treatment is based on their race?¹⁰

The idea of different racial categories has received strong criticisms.¹¹ The information gained from looking at genetic variances shows cross-racial similarities and differences.¹² As advances are made in science through the use of genetics, self-identifiable classifications are losing their utility in medicine.¹³ For example, doctors have discovered that the sickle cell trait is not exclusive to people of African origin, but also can be found in people of Mediterranean and Indian origin.¹⁴

The advances made using gene research are leading to medication regimens that are customized to an individual's genetic makeup.¹⁵ Genetics is being used to analyze how an individual reacts to medications on a genetic level.¹⁶ Genetics was the tool that allowed doctors to identify the allele, HLA-B*5701, which causes a serious adverse reaction to the drug Abacavir in some patients.¹⁷ Now patients with the HLA-B*5701 allele know not to take Abacavir.¹⁸ This gives rise to the concept of "personalized medicine."¹⁹ This individualized practice of medicine "seeks to harness . . . knowledge" by subjecting a patient to testing whether a medication will confer a benefit before it is prescribed and determining the dosage to prescribe.²⁰ Personalized medicine may lead to a day where someone's racial classification will be of no consequence when suggesting a treatment regimen.²¹

* Roxanne Melvin is a 2013 JD candidate at American University Washington College of Law. She received her BA from the University of Florida. She is currently a note and comment editor for the *Administrative Law Review*. She would like to thank Professors Robert G. Vaughn and Darren Hutchinson for their advice and feedback on this Comment. She would also like to thank her family, Louis Piper, Sr., for being an endless source of support and encouragement and, Louis Piper, Jr., for being a constant reminder to persevere in the face of adversity and view obstacles as opportunities that open doors.

This Comment will address how the FDA, using its current regulatory framework, can play a role in the advancement of the idea of personalized medicine when race is at issue. Specifically, this Comment will examine the role of the FDA in determining whether to approve drugs that failed to show effectiveness in the general population, and the maker of the drug is prompted to do a new clinical trial based on race after doing a retrospective analysis to ascertain which groups the drug actually benefited.²² Section I will provide scientific background and will cover the progression of personalized medicine starting with the controversies surrounding the drug BiDil and then will move on to cover the use of Pharmacogenomics (PGx) and Pharmacogenetics (PGt). Section II will propose recommendations to the FDA when dealing with race-specific approvals. Section III will provide justification for these recommendations and discuss the constitutionality and social implications of race-specific drug approvals, mainly concerned with how this practice can lead to others being treated differently based on their race. Finally, this Comment will conclude by emphasizing the additional requirements the FDA should request when evaluating applications from companies that want to reapply to save a failed drug.

I. THE PROGRESSION OF PERSONALIZED MEDICINE

A. Arguable Shortcut to Personalized Medicine: Revisiting the Approval of BiDil

In 2005, BiDil was the first drug to be approved by the FDA on the basis of race.²³ It was approved only to treat self-identified black patients with heart disease²⁴ by increasing the levels of nitric oxide providing assistance for the heart to pump blood.²⁵ Further investigation, however, has shown that Dr. Jay Cohn was using the drug to treat patients since the 1980s without mention of a targeted race.²⁶ In fact, the 1987 patent Dr. Cohn filed is devoid of a racial component.²⁷ As the original patent was set to expire in 2007, Dr. Cohn filed a new patent in 2000, but this time mentioning its use for treatment of African Americans.²⁸

BiDil was created in 1978 by Dr. Jay Cohn when he started using two existing drugs, hydralazine and isosorbide dinitrate, to increase nitric oxide in the blood of heart failure patients.²⁹ From 1980 to 1991, BiDil was tested in two clinical trials called V-HeFT I and V-HeFT II.³⁰ In V-HeFT I, it seemed to reduce the mortality rate of heart disease; however, in V-HeFT II, when it was compared to an existing drug on the market, the existing drug showed a greater reduction in mortality.³¹

After the V-HeFT clinical trials were completed, Dr. Cohn sought approval for BiDil from the FDA in 1997; however, the FDA denied the new drug application.³² Members on the committee pointed out that Enalapril, one of the already existing treatments for heart failure, was better at treating heart failure than BiDil.³³ One member on the committee called Enalapril superior to BiDil, and another member expressed doubt about whether BiDil had any overall benefit when compared to Enalapril.³⁴ After failing to secure FDA approval, Dr. Cohn, through a retrospective analysis of the clinical trials, noticed

that isolating the results in the African-American patients made the drug look like it could be more effective in African-Americans than Caucasians.³⁵ He mentioned that 70 percent of the participants were Caucasian in both trials, and African-Americans were a sizeable amount of the rest of the participants.³⁶

If the drug response in Caucasians included in the study was taken out of the results, BiDil looked to be more effective.³⁷ After failing the first attempt at FDA approval, Dr. Cohn applied for a new patent, this time stating that BiDil was to be used for treating heart failure in African-Americans.³⁸ He approached the FDA with the results from the V-HeFT trials.³⁹ With the help of the FDA, plans for a new clinical trial were formulated.⁴⁰ Results showing that African-Americans fared better on BiDil justified another trial called A-HeFT that only enrolled self-identified African-Americans.⁴¹ NitroMed, the company associated with Dr. Cohn, suggested that the reason African-Americans fared better on the drug than Caucasians “might be due to ‘a pathophysiology found primarily in black patients that may involve nitric oxide insufficiency.’”⁴² Dr. Cohn received affirmation from the FDA that a positive response in African Americans would result in approval for black patients.⁴³ When the A-HeFT trial started, in July 2001 to July 2004, the results of the A-HeFT trial indicated a favorable reduction in mortality for patients taking BiDil.⁴⁴ Based on the results from the trial, the Cardiovascular and Renal Advisory Committee (CRAC) of the FDA notified NitroMed of the possibility of early termination of the trial.⁴⁵

When the CRAC met on June 16, 2005, the vote was to approve BiDil for use in black patients with heart failure.⁴⁶ BiDil became the first drug ever to be approved for only one race.⁴⁷ However, some members of CRAC expressed reservations about putting a race limitation on the drug.⁴⁸ The concern with labeling the drug for use in only black patients was that it could be misconstrued as having a biological basis and no explanation was offered for the reasoning behind it.⁴⁹ Dr. Ota Wang pointed out that the A-HeFT study was prefaced on biology; however, the biological evidence was lacking.⁵⁰

Once the news of BiDil’s approval for use in only black patients disseminated, Dr. Ota Wang’s concerns relating to labeling were echoed by commentators, critics, and skeptics.⁵¹ One article on BiDil argued that NitroMed and the FDA used race as a proxy for a deficiency in nitric oxide because it was easier than developing a genetic test.⁵² Another warned that black patients could suffer as physicians start to replace leading drugs with drugs that purport to be effective in a specific race.⁵³ However, some saw the A-HeFT trials and BiDil as fulfilling an unmet medical need.⁵⁴

B. Genetic Focused Approach to Personalized Medicine

The study of Pharmacogenomics (PGx) and Pharmacogenetics (PGt) is the crux of the concept that personalized medicine can provide precision in treating disease.⁵⁵ Individuals are affected differently by diseases and can react to drugs varyingly for a multitude of reasons.⁵⁶ Genetics can cause varied drug interaction.⁵⁷ PGx looks at how genetic variations affect the pharmacokinetics,

drug exposure, and pharmacodynamics, drug response, in different individuals.⁵⁸ PGx examines what gene or genes are affected by a drug's pharmacokinetics; explores how the drug is metabolized, absorbed, distributed, and excreted (ADME); and studies pharmacodynamics, looking at the differences in the physiologic and pathologic response to a drug.⁵⁹

PGt is the study of genetically testing individuals for therapeutic reasons.⁶⁰ It tests for polymorphisms and genetic mutations.⁶¹ Looking at these key aspects of drug response on the genetic level allows for the creation of a more effective drug regimen.⁶² The drug regimen is more effective because it will be known, before prescribing a drug, if the drug will result in an adverse reaction in the patient, a placebo effect, or will be effective for that individual.⁶³

C. Personalized Medicine Using Pharmacogenetics: A Look at Herceptin and Inform Dual ISH

The effective use of Herceptin is an example of how personalized medicine can add customization and accuracy to treatment of breast cancer. Some women with breast cancer overexpress a gene called HER2.⁶⁴ The drug Herceptin can be used to treat these cancer patients.⁶⁵ On June 14, 2011, the FDA approved a PGt test called Inform Dual ISH that enables the user to count the number of chromosome 17—where the HER2 gene is located—and HER2 genes.⁶⁶ A doctor treating a breast cancer patient can now personalize the drug regime for a patient by administering the Inform Dual ISH test to determine if HER2 is being overexpressed and deciding if the patient will be a good candidate for Herceptin.⁶⁷

Race can be an indicator of the probability that a patient may have a disease or that a certain drug will help; however, relying on race misses the fact that a disease or treatment may still occur or be useful in other populations.⁶⁸ For instance, in a study conducted on the HER2 gene expression in uterine serous papillary cancer, it was found that 70 percent of black women showed heavy staining of HER2 compared to 24 percent of white women.⁶⁹ In a hypothetical where 70 percent of black women with breast cancer overly express HER2 versus 24 percent white women, it would appear Herceptin is ineffective due to the negative response or non-response in white women eclipsing the beneficial response in black women if the FDA and drug manufacturer were unaware of the HER2 gene overexpression.⁷⁰ This example highlights the utility of PGx and PGt study and the loss sustained when pharmaceutical researchers shortcut genetic investigation by using race as a substitute.⁷¹

The study of PGx and PGt highlights that genetic investigation is far more exact than using race.⁷² Since the 1970s, it was common knowledge in the scientific community that race only accounts for a small amount of genetic variation.⁷³ There is a loose correlation between race and disease, and genetics can have a wide variance within the same race.⁷⁴

However, race has a place in medicine because race is important to evaluate health care disparities.⁷⁵ When race is accounted for, discovery of unequal medical treatment among different racial groups can be made.⁷⁶ One study that evaluated physicians'

recommendations to patients who were actors complaining of symptoms of coronary artery disease revealed that physicians were less likely to recommend cardiac catheterization for women and African-Americans.⁷⁷ Collecting data by pharmaceutical companies on race is helpful in identifying whether there are trends in exclusion of certain races from clinical trials.⁷⁸ In fact, the FDA can actually put a hold on an investigational new drug application if the company is excluding people who are eligible to be included in a clinical trial based on a potential or perceived risk.⁷⁹

One of the shortfalls to the BiDil clinical trials was that in the thirty-three years of its creation and use, no attempt was made to do a PGx test on it.⁸⁰ Clyde Yancy, a cardiologist on the A-Heft steering committee, acknowledged genomics had given insight.⁸¹ He noted that BiDil is more effective in African-Americans than Caucasians because it enhances nitric oxide; however, there was no mention of a test conducted to validate the claim or any mention of PGx data being gathered.⁸²

II. Narrowly Tailoring Approvals of Raced Based Medicines

A. What Goes into Getting a Drug Approved

Before a new drug can be marketed in the United States, the drug manufacturer must first perform lengthy laboratory and animal tests.⁸³ Then the drug is tested in humans.⁸⁴ Before the drug is marketed to the public, the company must apply with the FDA and be approved.⁸⁵ A report from a clinical trial showing the drug is safe and effective in its use is needed.⁸⁶ On average, it takes twelve years and millions of dollars to bring a drug from laboratory to pharmaceutical availability.⁸⁷ Throughout the new drug application, the company meets with the FDA to discuss design and size of the clinical trial of the drug.⁸⁸ These meetings give a drug company the opportunity to address questions that the FDA may have when a new drug application is being reviewed.⁸⁹

A drug goes through either four phases or a blend of the four phases.⁹⁰ In Phase 0, in vitro testing determines toxicity, binding, and other parameters.⁹¹ The drug is then tested in animals to ensure safety and effectiveness.⁹² An investigational new drug application is submitted to the FDA to get approval for human studies to be conducted.⁹³ In Phase 1, the drug is tested in a small number of humans.⁹⁴ During this phase, the drug is given in low doses to determine the drug's pharmacological effects.⁹⁵ Phase 2 testing is conducted on several hundred participants in a well-controlled, closely monitored study.⁹⁶ Finally, Phase 3 testing involves expanded controlled and uncontrolled studies that obtain more information on the safety and effectiveness of a drug and gauges how the drug will affect the general population.⁹⁷ If adequate testing by all reasonably controlled methods does not show that the drug is safe and effective for use under the conditions in the proposed label, then the FDA can deny the application.⁹⁸

When a clinical trial is conducted, the FDA does not mandate by statute or regulation that there be a specific racial composition.⁹⁹ However, the FDA requires data on the racial composition of a clinical trial.¹⁰⁰ The FDA has the power to place holds on an investigational

new drug application,¹⁰¹ which stops or delays a clinical trial until the offending issue is fixed and the order is removed.¹⁰² Additionally, the commissioner of the FDA promulgates rules, bolstered by the force of law for the FDA's enforcement.¹⁰³ The FDA can issue non-legally binding guidance as it sees necessary to show what it thinks a statutory or regulatory requirement means and how to comply.¹⁰⁴ For instance, in February 2011, the FDA released a guidance document on when genomic information should be used during drug development; however, the guidance somewhat impeded the focus on genetics by stressing that attention should be paid to varying effects in different racial groups.¹⁰⁵

B. Broadening the Scope of Safety

The FDA was created by and receives its regulatory authority from the Federal Food, Drug and Cosmetic Act of 1938.¹⁰⁶ If the FDA determines a drug is not "safe for use under the conditions of use prescribed, recommended, or suggested," it will deny the application for that drug.¹⁰⁷ However, the definition of safety was not established in the act, and the FDA has not stated the criteria for establishing safety.¹⁰⁸

The field of PGx and PGt is still evolving.¹⁰⁹ More research is required to use genomic information in medicine to its full extent.¹¹⁰ There will be instances where the genetic information will be unavailable in a drug analysis,¹¹¹ but without any incentive to do PGx research, some companies may never invest the time or financial resources to understand why and how the drug it has created works genetically.¹¹² The FDA should require companies who reapply on racial grounds, after failing due to safety issues or lack of efficacy, to prove they attempted to gain a PGx and PGt understanding of the drug.¹¹³

The FDA should carefully scrutinize race-based drug approval applications and broaden the scope of safety to include issues such as the effects on potentially excluding a racial group from use when dealing with race-based drug applications.¹¹⁴ Currently, the FDA considers non-response to a drug to be an issue of effectiveness.¹¹⁵ However, according to Barbara J. Evans, professor of law at the University of Houston Law Center, non-response to a drug can also be a safety issue.¹¹⁶ Non-response to a drug is an opportunity cost that results from losing the chance to take another drug that could have offered a therapeutic benefit.¹¹⁷ Evans takes the lost chance concept from the lost-chance doctrine, where some states allow patients to bring tort suits because of untimely diagnosis or negligent treatment.¹¹⁸ The lost chance concept illustrates the safety issues surrounding a poorly targeted drug.¹¹⁹

In light of "lost chance" effects on safety, the FDA should require companies requesting approval of race-specific drugs to provide more information on attempted genetic studies.¹²⁰ In the case of a race-specific drug, there may be harm to the race for which it was not approved.¹²¹ Since the impetus to conduct a race-specific study will most likely be a retrospective analysis of the data gathered from a trial that has already been done, it is highly unlikely that there will be equal representation from all races in the original study.¹²²

Thus, other races may actually benefit from the drug but may not attempt to take it because of the race-specific approval. By requiring a company to show it attempted to do a PGx and/or PGt analysis, it will reduce lost chance effects where possible.¹²³

This approach may incentivize pharmaceutical companies to collect genetic information at the onset of drug development and clinical testing; however, the pharmaceutical companies would undeniably have to attempt to acquire the information if they are trying to save a failed drug.¹²⁴ If pharmaceutical companies with failed drugs have PGx information, they may be able to save the drug by retesting based on genetics; however, if using race is allowed, pharmaceutical companies will take the cheaper shortcut.¹²⁵ If the FDA employed this new model of regulating failed new drug applications, it would lead to more advances in PGx and make drugs more efficient because they will be properly targeted.¹²⁶

This proposal is not unattainable or too costly.¹²⁷ It is supported by a 2006 report in the *New York Times* showing that sales for BiDil were slow.¹²⁸ In the wake of slow sales, NitroMed attempted to acquire more genomic information.¹²⁹ The company started collecting genetic data from 358 patients who participated in A-HeFT.¹³⁰ The later analysis detected three gene variations that may affect BiDil's response in patients.¹³¹ NitroMed announced that diagnostic testing for the drug may be a possibility and will be assessed after more genomic analysis is done.¹³² Ultimately, if a pharmaceutical company has a financial incentive to conduct PGx studies, then it will.¹³³

C. More Inclusive Clinical Trials

In September 2005, the FDA released a guide with its recommendation for how to collect racial and ethnical data.¹³⁴ The FDA outlined the minimum categorical options that should be offered when collecting racial and ethnical data.¹³⁵ In cases where PGx information cannot be obtained, the FDA should allow the company to resort to race if the company can show it attempted to conduct separate clinical trials, each consisting of a homogeneous group of the minimum categorical options listed in the guidance.¹³⁶ The trials should be separate, distinct, and run simultaneously to ascertain how each group reacted to the drug. This requirement would help to minimize the negative impacts on groups that are excluded from the FDA approved use.¹³⁷ The label following approval should use language such as "most commonly effective in" and avoid language like "almost exclusively."¹³⁸

III. ISSUES WITH NOT ATTEMPTING TO NARROWLY TAILOR RACE-BASED PERSONALIZED MEDICINE

A. Violating the Fifth Amendment

If the FDA does not undertake further investigation in instances where a company is using race as a basis for getting a drug approved, there are potential constitutional issues.¹³⁹ Some commentators have suggested that race-based drug approvals may violate the Fourteenth Amendment's Equal Protection Clause.¹⁴⁰ When the FDA approves a drug for a certain use, an insurance company often reimburses the

prescription payment when a doctor prescribes a medication to a patient for the intended use.¹⁴¹ Many times, an insurance company may not reimburse for experimental or investigational drugs, which may include off-label uses, because of the policy that insurance is for FDA-approved care.¹⁴² If an insurance company will not reimburse an unapproved race using a race-specific drug, then a government action has caused an individual to pay more based on their race.¹⁴³ Not only has a government action caused the individual to be treated differently, but the individual has also been forced to pay more for something on account of race which amounts to a deprivation of property.¹⁴⁴ The deprivation of property and race-based differential treatment implicates the equal protection component of the Fifth Amendment.¹⁴⁵

The Fifth Amendment is also applicable to actions taken by the federal government.¹⁴⁶ The Amendment states “No person shall . . . be deprived of life, liberty, or property, without due process of law.”¹⁴⁷ In *Bolling v. Sharpe*,¹⁴⁸ the Supreme Court held that, although the Fifth Amendment did not have an Equal Protection Clause like the Fourteenth Amendment, the concepts of Due Process and Equal Protection were not mutually exclusive.¹⁴⁹ In *Bolling*, a case about segregation in public schools in the District of Columbia, the Court discussed the limits that the Fifth Amendment’s Due Process clause places on race-based policymaking:

Liberty under law extends to the full range of conduct which the individual is free to pursue, and it cannot be restricted except for a proper governmental objective. Segregation in public education is not reasonably related to any proper governmental objective, and thus it imposes on Negro children of the District of Columbia a burden that constitutes an arbitrary deprivation of their liberty in violation of the Due Process Clause.¹⁵⁰

Arguably, the government has a proper objective in improving the health of the group the drug is approved for; however, if the head of the FDA is acting within the scope of power granted, a court could analyze whether the action taken was arbitrary, capricious, or an abuse of discretion.¹⁵¹ It could be contended that without requiring a drug company seeking to get a race-based drug approved to show it exhausted all other possible alternatives to race, the approval is arbitrary and capricious.¹⁵² Since the Supreme Court has given guidelines on how to constitutionally use race, the FDA should expand its scope of safety to ensure its decision to approve a race-based drug would withstand a constitutional challenge.¹⁵³ Following the same analysis of the Court in *Bolling*, the government cannot deprive an individual of property without a proper governmental objective.¹⁵⁴ Debatably, approving a race-specific drug application to improve the health of one group at the expense of others may not be a proper governmental objective since it is burdensome and arbitrarily treats the excluded groups unfairly in violation of the Fifth Amendment.¹⁵⁵ By broadening the scope of safety, the FDA would prove the government is not arbitrarily or capriciously depriving individuals of their property based on race.¹⁵⁶

B. Social Implications

Many experts acknowledged that race is socially constructed.¹⁵⁷ The position taken is that race is a political system grouping people socially based on invented criteria.¹⁵⁸ Perhaps societal issues are outside the scope of the FDA’s purview; however, the FDA should keep them in mind when making decisions and not allow race to be used as a shortcut to understanding biology and genetics in drug approvals.¹⁵⁹ Even the Health and Human Services Department drafted a report asking the FDA to encourage gene-based studies over race-based ones.¹⁶⁰ The danger is that allowing race-based shortcuts gives credence to the idea of race-based diseases or drugs.¹⁶¹

Some critics of PGx say that too much focus on genetics will disincentivize society from fixing potential underlying issues.¹⁶² They fear that instead of fixing catalytic factors such as, inter alia, social, economic, and environmental inequalities, the solution will be to sell expensive drugs.¹⁶³ For instance, a study conducted in Puerto Rico showed a correlation with high systolic blood pressure (SBP), socio-economic status, and skin color.¹⁶⁴ In Puerto Rico, different skin tones and facial features have different cultural classifications.¹⁶⁵ The lightest skin tones are called *blanco*, medium skin tones are called *trigueño*, and dark skin tones are called *negro*.¹⁶⁶ The study found that people with the classification of *negro* had the highest SBP and *blanco* classification had the lowest as socio-economic status increased.¹⁶⁷ The results indicated that socioeconomic and cultural factors are most likely the culprits of the disparity.¹⁶⁸ People at the lower end of the societal spectrum do not experience as many stressors from race as people at the higher end of the societal spectrum.¹⁶⁹ Continuous exposure to pressures from racism can result in high blood pressure as well as other cardiovascular reactions.¹⁷⁰ An increased focus on genetics will not lead to the effects of other factors, in this case cultural, eluding society with an expensive drug standing in substitution as a cure for the cultural problem. For example, genetic research led to the finding that sickle cell was not exclusive to African descendants and that the trait protects against malaria, a negative environmental factor.¹⁷¹

CONCLUSION

When the FDA is dealing with race-specific drug approval requests, in which a retrospective analysis shows the drug fared better in one race over another, the FDA should require the drug maker to show that a PGx analysis was done on the drug. If the technology does not exist to do a PGx study on the drug, the FDA should only approve drugs based on race when the company shows it did an inclusive clinical trial consisting of the minimum ethnic classifications listed in the FDA’s guidance to minimize the number of groups excluded from use of a drug. When race is the basis of a drug approval application, the FDA should broaden its scope of “safety” to include lost chances to individuals of excluded groups that may have been able to benefit, and include groups that forgo the leading alternative based on the fact that the drug is approved for use solely in that group.

The FDA will be able to expand the scope of safety when asked to make race-based approvals because to do otherwise may meet constitutional challenges. Expanding the scope of safety will allow the FDA to prove its decisions for approving a race-specific drug are not made arbitrarily or capriciously. Furthermore, carefully scrutinizing race-based approvals is also socially responsible. In 2011, when the FDA came out with its guidance on PGx, it left the door open for race-based shortcuts by encouraging the collection of PGx data but not requiring it for race-based approvals. With the 2011 approval of Inform Dual ISH test and advances being made in the field of PGx and PGt, it is time the FDA closed the door to race-based shortcuts.

¹ See generally Alana Patrick, *UC Berkeley "Racist" Bake Sale Sparks Controversy*, HUFFPOST COLLEGE, (Oct. 5, 2011, 12:50 PM), http://www.huffingtonpost.com/uloop/uc-berkeley-racist-bake-sale_b_995031.html (reporting that a student group at UC Berkeley provoked intense controversy when it based the cost of its baked goods on the race of the customer).

² See *id.* (noting that the student's justification of the pricing scheme was to "ensure the fairest distribution," and to guarantee that "a DIVERSE population of RACES of students" get to enjoy the baked goods).

³ See generally Holly Yan, *Pay-by-race Bake Sale at UC Berkeley Still On, Student Republican Group Says*, CNN U.S., (Sept. 26, 2011), http://articles.cnn.com/2011-09-26/us/us_california-racial-bake-sale_1_bake-sale-baked-goods-cookie-sale?s=PM:US (explaining that the bake sale was meant to be racist and discriminatory to draw attention to legislation that would allow California universities to consider race, gender, ethnicity, and national origin during the admissions process).

⁴ See AARP, *PRESCRIPTION DRUG COSTS AND THE ROLE OF GENERIC DRUGS: PUBLIC OPINION AMONG AMERICANS AGED 45 AND OLDER* (2002) (surveying Americans forty-five and older, who report nine out of ten times they would like to reduce out of pocket expenses).

⁵ See Press Release, U.S. Food & Drug Admin., *FDA Approves BiDil Heart Failure Drug for Black Patients* (June 23, 2005), available at <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2005/ucm108445.htm> (announcing that BiDil was approved to be used in remedying heart failure in self-identified black patients, thereby representing a step closer towards personalized medicine); see also Joshua Cohen, *Off-Label Use Reimbursement*, 64 FOOD & DRUG L.J. 391, 394–95 (2009) (showing that off-label prescriptions may not be reimbursed by health insurance).

⁶ See *id.* (declaring that BiDil "is a striking example of how a treatment can benefit some patients even if it does not help all patients").

⁷ See *id.* (stating that the Food and Drug Administration (FDA) hopes to find a process to identify people of other races that the drug will help).

⁸ See Elizabeth Landau, *How Medicine is Advancing Beyond Race*, CENTER FOR GENETICS & SOC'Y (Aug. 31, 2011, 9:55 PM), <http://www.geneticsandsociety.org/article.php?id=5786&printsaf=1> (mentioning that the ability to look at genetic variations is diminishing the utility of race since genetic markers and the way individuals self-identify do not always match up).

⁹ See David E. Winickoff & Osagie K. Obasogie, *Race-Specific Drugs: Regulatory Trends and Public Policy*, 29 TRENDS IN PHARMACOLOGICAL SCI. 277, 278 (2008) (calling for strict scrutiny when dealing with drugs designed for a specific race).

¹⁰ See 21 U.S.C. § 355 (2002) (defining the grounds on which the FDA can refuse an application for drug approval).

¹¹ See DOROTHY ROBERTS, *FATAL INVENTION: HOW SCIENCE, POLITICS, AND BIG BUSINESS RE-CREATE RACE IN THE TWENTY-FIRST CENTURY* 4 (2011) (stating that the creation of race is a political practice).

¹² See Osagie K. Obasogie, *Playing the Gene Card? A Report on Race and Human Biotechnology* (Center for Genetics and Society, Oakland, Cal.), 2009, at 1, 12 (stating that "there is little robust evidence that race is a suitable proxy for genetic differences in drug response").

¹³ See Landau, *supra* note 8 (noting that if a physician could look at the patient's entire genome and identify genetic variants, then race would become

far less important to clinical medicine since the relationship between race and disease is imperfect).

¹⁴ *Id.*

¹⁵ See *cf.* FOOD & DRUG ADMIN., *GUIDANCE FOR INDUSTRY CLINICAL PHARMACOGENOMICS: PREMARKETING EVALUATION IN EARLY PHASE CLINICAL STUDIES DRAFT* (2011) [hereinafter *GUIDANCE*] (noting that knowing genomic information during drug development can help improve the effectiveness and safety of drugs).

¹⁶ *Id.*

¹⁷ *Id.*

¹⁸ *Id.*

¹⁹ See Barbara J. Evans, *What Will It Take to Reap the Clinical Benefits of Pharmacogenomics?*, 61 FOOD & DRUG L.J. 753 (2006) (explaining that personalized medicine uses genetic tests before prescribing medication to determine the benefits and appropriate dosage for the medication).

²⁰ *Id.*

²¹ See Andrew Pollack, *Despite Gene Patent Victory, Myriad Genetics Faces Challenges*, CENTER FOR GENETICS & SOC'Y (SEP. 14, 2011, 5:25 PM), <http://www.geneticsandsociety.org/article.php?id=5831&printsaf=1> (discussing that DNA-sequencing has become faster and cheaper and will soon be able to sequence the entire genome).

²² See Press Release, *supra* note 5 (noting that earlier trials of BiDil showed no benefit in the general population but benefits seen among self-identified blacks prompted a new trial for just this group); see also Stephanie Saul, *F.D.A. Approves a Heart Drug for African-Americans*, N.Y. TIMES, JUNE 24, 2005, at C2.

²³ See Arlene Ducao, *BiDil, A-HeFT, and the Future of Race in Pharmacogenetics/genomics*, KAON NA (Sept. 2, 2011, 5:29 PM), <http://www.arlduc.org/word/BiDilDraft02.html> (recalling FDA's approval of the first drug catering to a specific race).

²⁴ See *id.* (announcing the approval of BiDil for self-identified black patients); see also Stephanie Saul, *F.D.A. Approves a Heart Drug for African-Americans*, N.Y. TIMES, JUNE 24, 2005, at C2 ("The Food and Drug Administration took a controversial step . . . approving the first drug ever intended for one racial group, African-Americans.").

²⁵ See Stephanie Saul, *2 Officials Quit Amid Slow Sales of Heart Drug for Blacks*, N.Y. TIMES, MARCH 22, 2006, at C2 (stating that Dr. Cohn created BiDil from two generic drugs that combined increases nitric oxide in the blood aiding the heart to pump).

²⁶ Stephanie Saul, *F.D.A. Approves a Heart Drug for African-Americans*, N.Y. TIMES, JUNE 24, 2005, at C2 (stating that in the 1980's Dr. Jay N. Cohn began using the drug with patients in various veterans' hospitals with no mention of it being race-specific); see also Pamela Sankar & Jonathan Kahn, *BiDil: Race Medicine or Race Marketing?*, Academic Ventures (last visited Apr. 15, 2012, 1:26 PM), <http://www.academicventures.com/elsi/Abstracts/handouts/H-4%20Sankar.kahn.bidil.pdf> ("The 1987 methods patent . . . was not race-specific.").

²⁷ See U.S. Patent No. 4,868,179 (filed April 22, 1987) (requesting a patent for a drug to be used to treat patients with chronic congestive heart failure but lacking mention of race).

²⁸ See U.S. Patent No. 6,465,463 (filed Sept. 8, 2000) (requesting a patent for a drug to be used to treat African-American patients with heart failure).

²⁹ See also Ducao, *supra* note 23 (stating that Dr. Cohn discovered BiDil in 1978 when he combined two existing heart failure drugs and began using it on patients at various veterans' hospitals).

³⁰ *Id.*

³¹ See Rene Bowser, *Race as a Proxy for Drug Response: The Dangers and Challenges of Ethnic Drugs*, DEPAUL L. REV. 1111, 1117 (2004) (stating that in the first trial BiDil seemed to be reducing heart disease deaths, but in the second trial it did not meet the current standard).

³² See FOOD & DRUG ADMIN. CTR. FOR DRUG EVALUATION & RESEARCH EIGHTIETH MEETING OF THE CARDIOVASCULAR & RENAL DRUGS ADVISORY COMM. (1997) 139-40 [hereinafter *MEETING*], available at <http://www.fda.gov/ohrms/dockets/ac/97/transcript/3264T1.pdf> (voting no to the question of whether there was statistically significant effects on mortality during the V-HeFT I study).

³³ See *id.* at 97 (discussing the opinions of Dr. Thadani and Dr. Lindenfeld regarding Enalapril as opposed to BiDil). Dr. Thadani noted that Enalapril was superior to BiDil in clinical trials and Dr. Lindenfeld expressed disbelief

that BiDil had any overall benefits compared to Enalapril). *Id.* at 183-85.

³⁴ *Id.* at 173.

³⁵ See *id.* at 20-21 (recording that Dr. Cohn gathered data on the Caucasian versus African-American response to BiDil); see also Jonathan Kahn, *From Disparity to Difference: How Race-Specific Medicines May Undermine Policies to Address Inequalities in Health Care*, 15 S. CAL. INTERDISC. L.J. 105, 111-12 (2005) (noting that the 1997 new drug application was rejected and the results from the V-HeFT trials were re-categorized according to race).

³⁶ *Id.* at 20-21.

³⁷ See MEETING, *supra* note 32.

³⁸ See U.S. Patent No. 6,465,463 (filed Sept. 8, 2000) (asserting that the invention was for treatment and prevention of mortality due to heart failure in African-Americans).

³⁹ See DEP'T OF HEALTH & HUMAN SERVICES FOOD & DRUG ADMIN. CTR. FOR DRUG EVALUATION & RESEARCH CARDIOVASCULAR & RENAL DRUGS ADVISORY COMM., 13 (June 16, 2005), available at <http://www.fda.gov/ohrms/dockets/ac/05/transcripts/2005-4145T2.pdf> (acknowledging that the FDA was approached by Dr. Cohn with the results from the V-HeFT trials).

⁴⁰ See *id.* at 28 (noting that the FDA helped with the black patients only clinical trial plan, with understanding that a positive response in African-Americans would result in approval).

⁴¹ *Id.* at 60.

⁴² Jonathan Kahn, *Getting the Numbers Right: Statistical Mischief and Racial Profiling in Heart Failure Research*, 46 PERSPECTIVES IN BIOLOGY & MED. 473, 474 (2003).

⁴³ DEP'T OF HEALTH & HUMAN SERVICES FOOD & DRUG ADMIN. CTR. FOR DRUG EVALUATION & RESEARCH CARDIOVASCULAR & RENAL DRUGS ADVISORY COMM., *supra* note 39, at 13.

⁴⁴ *Id.*

⁴⁵ See *id.* at 67 (stating unanimously the committee said to stop the trial based on favorable findings).

⁴⁶ See *id.* at 384-402 (voting that BiDil should be approved).

⁴⁷ See Saul, *supra* note 26, at C2 (announcing that BiDil is approved for use in black patients with heart failure).

⁴⁸ See DEP'T OF HEALTH & HUMAN SERVICES FOOD & DRUG ADMIN. CTR. FOR DRUG EVALUATION & RESEARCH CARDIOVASCULAR & RENAL DRUGS ADVISORY COMM., *supra* note 39, at 401 for an expression of concern by Dr. Ota Wang that because of the lack of explanation behind the rationale, the race specific approval could be interpreted as a biological reason.

⁴⁹ *Id.*

⁵⁰ *Id.*

⁵¹ See, e.g., Dov Greenbaum, *Incentivizing Pharmacogenomic Drug Development: How the FDA can Overcome Early Missteps in Regulating Personalized Medicine*, 40 RUTGERS L.J. 97, 107 (2008) (pointing out that biological differences were not fully understood or accounted for).

⁵² *Gray Area for New Heart Failure Drug*, HARV. HEART LETTER (HARVARD MEDICAL SCHOOL, BOSTON, MASS.), Nov. 2005, at 1, 2 (suggesting that race was used as a "stand-in" because it was easier to ask individual their race than to spend money developing a test).

⁵³ See Bowser, *supra* note 31, at 1123 (lambasting that the ACE inhibitor substitution with BiDil will most likely lower the standard of care in black patients).

⁵⁴ See Andrew Pollack, *Drug Approved for Heart Failure in Black Patients*, N.Y. TIMES, July 20, 2004, at C1 (quoting Dr. Yancy that there was an unmet medical need to understand heart failure in African-Americans).

⁵⁵ See Matthew Avery, *Personalized Medicine and Rescuing "Unsafe" Drugs with Pharmacogenomics: A Regulatory Perspective*, 65 FOOD & DRUG L.J. 37, 40 (2010) (defining Pharmacogenomics (PGx) as the study of how different gene expression, DNA sequencing, and gene copy number affects an individual's reaction to a drug).

⁵⁶ See Obasogie, *supra* note 12, at 12-13 (highlighting that environmental, socio-economic, geographic origin, genetics, and a multitude of other factors affect the causes of disease).

⁵⁷ See GUIDANCE, *supra* note 15, at 2-3, 8 (noting that studying gene interaction with different drugs can determine if the individual will have a drug-induced adverse event).

⁵⁸ See GUIDANCE, *supra* note 15, at 13-14 (discussing the aspects that PGx considers).

⁵⁹ See *id.* at 2 (highlighting the aspects of PGx). See also David S. Bailey et

al., *Pharmacogenomics – It's Not Just Pharmacogenetics*, 6 CURRENT OPINION IN BIOTECHNOLOGY 595, 595 (1998) (explaining the complexities of PGx).

⁶⁰ See FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY AND FDA STAFF PHARMACOGENETIC TEST AND GENETIC TESTS FOR HERITABLE MARKERS (2007) (differentiating PGT testing from genetic testing).

⁶¹ See *id.* (explaining what PGT tests).

⁶² See GUIDANCE, *supra* note 15, at 5-7 (acknowledging that at times an allele can be the cause of an adverse reaction to a drug so a patient would know he or she should not take that particular drug).

⁶³ *Id.*

⁶⁴ See Press Release, U.S. Food & Drug Admin., FDA Approves New Test to Help Determine if Breast Cancer Patients are Candidates for Herceptin Treatment (June 14, 2011), available at <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm259055.htm> (explaining that some breast cancer patients are HER2-positive which makes them candidates for Herceptin).

⁶⁵ See DRUGS.COM, <http://www.drugs.com/pro/herceptin.html> (last visited Oct. 6, 2011) (discussing that Herceptin is used to block the growth of tumor cells that overexpress HER2).

⁶⁶ See Press Release, *supra* note 64 (explaining that the Inform Dual ISH test can allow chromosome 17 and HER2 genes to be counted on the same slide).

⁶⁷ See *id.* (releasing news that doctors can now test breast cancer patients to see if they are candidates for Herceptin treatment).

⁶⁸ See Obasogie, *supra* note 12, at 12 (advancing that root causes need to be examined to understand disease risks).

⁶⁹ See Alessandro D. Santin et al., *Racial Differences in the Overexpression of Epidermal Growth Factor Type II Receptor (HER2/neu): A Major Prognostic Indicator in Uterine Serous Papillary Cancer*, 192 AM. J. OF OBSTETRICS & GYNECOLOGY 813, 816 (2005) (reporting on the results of a study done comparing black and white women with uterine serous papillary cancer and the overexpression of HER2/neu).

⁷⁰ *Cf. id.*

⁷¹ See Landau, *supra* note 8 (explaining that the association between race and disease is too attenuated). *Contra* (countering importance of race to help focus outreach efforts).

⁷² See *id.* (quoting that genetic markers are loosely correlated with race because race was constructed artificially).

⁷³ See Jonathan Kahn, *Getting the Numbers Right: Statistical Mischief and Racial Profiling in Heart Failure Research*, 46 PERSPECTIVES IN BIOLOGY & MED. 473, 478 (2003) (noting that it has been known that race explains only a small amount of genetic variations and that individuals can vary more genetically with someone within the same race).

⁷⁴ See *supra* notes 73-74 and accompanying text.

⁷⁵ See BRIAN D. SMEDLEY ET AL., UNEQUAL TREATMENT: CONFRONTING RACIAL AND ETHNIC DISPARITIES IN HEALTH CARE 125-26 (2003) (discussing how some racial groups receive unequal medical treatment).

⁷⁶ *Id.*

⁷⁷ *Id.*

⁷⁸ See 21 C.F.R. pt. 312 (promulgating rules that the FDA can put a clinical hold on an investigational new drug application if the company is excluding individuals from clinical trials who would otherwise be eligible based on a perceived risk).

⁷⁹ *Id.*

⁸⁰ See Kahn, *supra* note 73, at 479 (writing that a cardiologist involved the A-HeFT study acknowledged in 2002 that "the emerging field of genomic medicine has provided insight into potential mechanisms to explain racial variability in disease [to] response to medical therapy").

⁸¹ *Id.*

⁸² See *id.*

⁸³ U.S. FOOD & DRUG ADMIN., DEVELOPMENT & APPROVAL PROCESS (DRUGS) <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/default.htm> (last visited March 23, 2013). Before a new drug application, all chemical entities in the drug must go through a investigational new drug process. A new chemical entity is studied for five to ten years. See Peter Barton Hutt et al., FOOD AND DRUG LAW 624 (Robert C. Clark et al. eds., 3rd ed. 2007) (discussing the procedures required for a manufacturer to demonstrate that a drug is both safe and effective).

⁸⁴ *Id.*

⁸⁵ 21 U.S.C. § 355(a) (2006).

- ⁸⁶ *Id.*
- ⁸⁷ *New Drug Approval Process*, DRUGS.COM, <http://www.drugs.com/fda-approval-process.html> (last visited March 23, 2012).
- ⁸⁸ See Peter Barton Hutt et al., *FOOD AND DRUG LAW* 626 (ROBERT C. CLARK ET AL. EDS., 3RD ED. 2007) (emphasizing that meeting with the FDA during the drug development process is critical to the success of a new drug application process).
- ⁸⁹ *Id.* at 683.
- ⁹⁰ See *id.* at 628–629 (acknowledging that over the years, the three distinct drug testing have broken down such that a drug can now be in multiple phases simultaneously).
- ⁹¹ *Id.*
- ⁹² *Id.* at 629.
- ⁹³ *Id.*
- ⁹⁴ See Hutt, *supra* note 88, at 630 (Phase 1 study usually has twenty to eighty participants).
- ⁹⁵ *Id.*
- ⁹⁶ *Id.* at 631.
- ⁹⁷ *Id.*
- ⁹⁸ 21 U.S.C. § 355(a) (2006).
- ⁹⁹ Hutt, *supra* note 88 at 645.
- ¹⁰⁰ *Id.* at 645–646.
- ¹⁰¹ See Hutt, *supra* note 88, at 636 (stating that the FDA uses holds to either stop clinical trials from beginning or halt trials already in progress).
- ¹⁰² *Id.*
- ¹⁰³ 21 C.F.R. § 10.40 (2010).
- ¹⁰⁴ See *id.* § 10.115 (establishing that the FDA can issue a guidance to put the public on notice of what it understands a statute or a regulatory issue to mean).
- ¹⁰⁵ See GUIDANCE, *supra* note 15 at 10 (“To design informative studies and interpret study results appropriately, careful attention should be given in clinical pharmacology studies to differences, if known, in the prevalence of ADME-related gene variants among racial or ethnically distinct groups.”).
- ¹⁰⁶ 21 U.S.C. 393 (2006) (“There is established in the Department of Health and Human Services the Food and Drug Administration.”).
- ¹⁰⁷ Hutt, *supra* note 88, at 685.
- ¹⁰⁸ *Id.*
- ¹⁰⁹ See Landau, *supra* note 8 (explaining that more research is needed to utilize all of the genomic sequencing information in medicine); see also Victoria M. Kumorowski, *Assessing Legal Liability in Pharmacogenetic Cases*, 42 WASHBURN L.J. 623, 623 (2003) (stating that science has unveiled that 99.9 percent of human DNA is identical and 0.1 percent accounts for differences).
- ¹¹⁰ Kumorowski, *supra* note 109, at 623.
- ¹¹¹ See *Mechanism of Action*, EXTRAORDINARY MED. THE TRUTH ABOUT HOMEOPATHY (SEP. 14, 2011, 4:35 PM), <http://www.extraordinarymedicine.org/2011/01/14/mechanism-of-action/> (highlighting that it is unknown why some drugs work; for instance, the mechanism of action in Aspirin was unknown until 1971 and the mechanism of action remains unknown in Tylenol).
- ¹¹² See Obasogie, *supra* note 12, at 13 (highlighting the fact that in 2004 it was reported that twenty-nine drugs claimed to be either more effective or safer in different racial groups).
- ¹¹³ See DRUGS.COM, <http://www.drugs.com/pro/bidil.html> (last visited Sept. 2, 2011) (reporting that a PK study was not complete on BiDil and the PD basis was not known). This illustrates that some companies are not incentivized to use PGx to understand how its drug works especially when they can use race as a shortcut.
- ¹¹⁴ See Winickoff & Obasogie, *supra* note 9, at 278 (calling for a strict scrutiny approach in deciding the kinds of evidence required before a labeling medication for a specific race).
- ¹¹⁵ See Evans, *supra* note 19, at 762 (stating that the FDA treats non-response as an issue with a drug’s effectiveness).
- ¹¹⁶ See *id.* at 762–63 (positing that non-response to a drug can be a safety issue because there can be harms associated with receiving no therapeutic benefit from a drug).
- ¹¹⁷ See *id.* at 763 n.37 (recognizing that, in some states, a patient can file a suit in tort for injuries sustained from an illness worsening due to negligent treatment or delay in diagnosis of the illness).
- ¹¹⁸ See Evans, *supra* note 19, at 763 (relating the idea of harm by foregoing other therapies to the Lost-chance doctrine).
- ¹¹⁹ See *id.* (showing that the FDA’s current methods undercount harm from progression on a disease due to a poorly targeted drug).
- ¹²⁰ See *id.* (stating that a “lost chance” injury occurs when a patient is hurt from a poorly targeted drug making the drug essentially unsafe).
- ¹²¹ See *id.*
- ¹²² See MEETING, *supra* note 32 (mentioning the racial makeup of the original BiDil study); see also *supra* Part IA.
- ¹²³ See *supra* Part IIB.
- ¹²⁴ See Matthew Avery, *Personalized Medicine and Rescuing “Unsafe” Drugs with Pharmacogenomics: A Regulatory Perspective*, 65 FOOD & DRUG L.J. 37, 38 (2010) (noting that there has been a decline in new drug approvals, resulting in an approval rate of less than 20 percent).
- ¹²⁵ See Obasogie, *supra* note 12, at 13 (highlighting that companies that have tried to save failed drug using race; for instance, there was an attempt to repackage Iressa for Asians).
- ¹²⁶ See Dov Greenbaum, *Incentivizing Pharmacogenomic Drug Development: How the FDA Can Overcome Early Missteps in Regulating Personalized Medicine*, 40 RUTGERS L.J. 97, 128 (2008) (stating that the FDA’s current regulations disincentive pursuance of PGx research); see also GUIDANCE, *supra* note 15, at 4 (noting that PGx can lead to greater knowledge of interindividual differences, can assist drug development, lead to the improvement, and greater safety of drugs).
- ¹²⁷ See Turna Ray, *HHS Draft Report Suggests Genetic Test for BiDil; NitroMed Does Not Rule Out Dx*, GENOMEWEB (SEPT. 2, 2011, 5:30 PM), <http://www.genomeweb.com/dxpgx/hhs-draft-report-suggests-genetic-test-bidil-nitro-med-does-not-rule-out-dx> (quoting that a NitroMed representative that diagnostic test are a possibility once more genomic research is done).
- ¹²⁸ See Saul, *supra* note 25, at C2 (reporting BiDil sales were off to a slow start and noting that a factor of its lackluster sales could be attributed to insurance reimbursement problems).
- ¹²⁹ Turna Ray, *supra* note 127.
- ¹³⁰ *Id.*
- ¹³¹ *Id.*
- ¹³² *Id.*
- ¹³³ See *supra* notes 127–132.
- ¹³⁴ See generally FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY COLLECTION OF RACE AND ETHNICITY DATA IN CLINICAL TRIALS (2005) (recommending that companies ask two preliminary questions: Hispanic or Latino, or Not Hispanic or Latino, and, when recording race and ethnicity, to offer the choices of American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or Other Pacific Islander, or White).
- ¹³⁵ *Id.*
- ¹³⁶ See GUIDANCE, *supra* note 135 (suggesting that a company collect at a minimum the racial and ethnical categories described in the guidance).
- ¹³⁷ See Jonathan Kahn, *From Disparity to Difference: How Race-Specific Medicines May Undermine Policies to Address Inequalities in Health Care*, 15 S. CAL. INTERDISC. L.J. 105, 111–12 (2005) (solving one of the problems with the A-HeFT trial). Because the A-HeFT trial lacked a population to compare it to the only real claim that can be made is “that . . . on the basis of [the] trials . . . BiDil works in some people who have heart failure, period.” See *id.* at 106.
- ¹³⁸ See generally Perry W. Payne, Jr., *For Asians Only? The Perils of Ancestry-Based Drug Prescribing*, RACE, PHARMACEUTICALS, & MED. TECH., 2008, at 585, 586 (criticizing the FDA for sending out an alert that a genetic variant was found “almost exclusively” in Asians, and arguing that the announcement created a new standard of care for doctors).
- ¹³⁹ See Winickoff & Obasogie, *supra* note 9, at 278 (mentioning potential Fourteenth Amendment Equal Protection Clause violation when government agency use race to determine drug approvals).
- ¹⁴⁰ *Id.*
- ¹⁴¹ See Cohen, *supra* note 5, at 394 (stating that insurance companies will often exclude reimbursement for FDA-unapproved care).
- ¹⁴² *Id.*
- ¹⁴³ See Erik Lillquist & Charles A. Sullivan, *The Law and Genetics of Racial Profiling in Medicine*, 39 HARV. C.R.-C.L. L. REV. 391, 445 (2004) (noting that the Equal Protection Clause of the Fourteenth Amendment is implicated when the government intentionally discriminates against a race).

¹⁴⁴ See *Adarand Constructors, Inc. v. Peña*, 515 U.S. 200, 200 (1995) (holding that race-based actions by the federal government needs to be strictly scrutinized).

¹⁴⁵ See Peter J. Rubin, *Taking its Proper Place in the Constitutional Canon: Bolling v. Sharpe, Korematsu, and the Equal Protection Component of Fifth Amendment Due Process*, 92 VA. L. REV. 1879, 1879 (2006) (describing that the Supreme Court cut an equal protection component out of the Due Process Clause of the Fifth Amendment).

¹⁴⁶ See *Barron v. Baltimore*, 32 U.S. (1 Pet.) 243 (1833) (stating that the Fifth Amendment should be interpreted as restricting the general power of the government, not the states).

¹⁴⁷ U.S. CONST. AMEND. V.

¹⁴⁸ 347 U.S. 497 (1954).

¹⁴⁹ *Id.* at 499.

¹⁵⁰ *Id.* at 499-500.

¹⁵¹ *Cf. Citizens to Preserve Overton Park v. Volpe*, 401 U.S. 402, 414 (1971) (stating that the reviewing court must set aside agency actions that are “arbitrary, capricious, [and] an abuse of discretion”).

¹⁵² *Cf. id.*

¹⁵³ See *supra* Part II (outlining steps the FDA can take to ensure its decisions survive constitutional challenges).

¹⁵⁴ *Cf. Bolling v. Sharpe*, 347 U.S. 497, 500 (1954) (stating that liberty cannot be restricted except for proper governmental objective).

¹⁵⁵ *Cf. id.*

¹⁵⁶ See *supra* Part II (explaining that the FDA could require a company to show before making a decision on a race-based drug application).

¹⁵⁷ See Roberts, *supra* note 11 (arguing that we use invented rules taught to us to assign racial designations, and that society determines the consequences based on the grouping).

¹⁵⁸ *Id.* at 4.

¹⁵⁹ See Ducao, *supra* note 23 (reporting that on worries in the scientific community about race “being used as a ‘crude marker’ for genetic and environmental factors.”)

¹⁶⁰ See Turna Ray, *HHS Draft Report Suggests Genetic Test for BiDil; NitroMed Does Not Rule Out Dx*, GENOMEWEB (SEPT. 2, 2011, 5:30 PM), <http://www.genomeweb.com/dxpgx/hhs-draft-report-suggests-genetic-test-bidil-nitromed-does-not-rule-out-dx> (noting that a report written by the Health and Human Services Department stated that BiDil’s label was “ambiguous and clinically sub-optimal”).

¹⁶¹ See Troy Duster, *Race and Reification in Science*, CENTER FOR GENETICS & Soc’y, (Aug. 31, 2011, 10:00 PM), <http://www.geneticsandsociety.org/article.php?id=1995> (making the argument that acceptance of categories of stored data sets would lead to a misconception of “black” or “white” diseases).

¹⁶² See Obasogie, *supra* note 12, at 14 (warning that genetic reductionism takes the focus off of societal factors and puts it on expensive medication).

¹⁶³ See *id.* (arguing that allowing biomedical companies to take over solving the problem of racial disparities in health diminishes the role of public health in addressing underlying social and environmental problems).

¹⁶⁴ See Clarence C. Gravlee et al., *Skin Color, Social Classification, and Blood Pressure in Southeastern Puerto Rico*, 95 AM. J. OF PUB. HEALTH 2191, 2194 (2005) (stating that the study’s findings suggested that the intersection of social and cultural factors relates skin color with blood pressure).

¹⁶⁵ *Id.*

¹⁶⁶ See *id.* at 2193 (outlining that the different cultural classifications given based on skin pigmentation and facial features).

¹⁶⁷ See *id.* at 2194 (reporting results from a study done to isolate the effects of skin color on blood pressure when skin color is used to determine social classification).

¹⁶⁸ See *id.* (noting that skin color is practically insignificant at the lower echelons of society, but racism is much more prevalent at the middle to higher echelons of society).

¹⁶⁹ See *id.* (discussing pressures from racism, including the manifestation of).

¹⁷⁰ See Gravlee, *supra* note 164.

¹⁷¹ Landau, *supra* note 8.